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MICROSCOPICAL STUDIES ON ABSCESS OF
THE LIVER

BY

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Fig. 1.

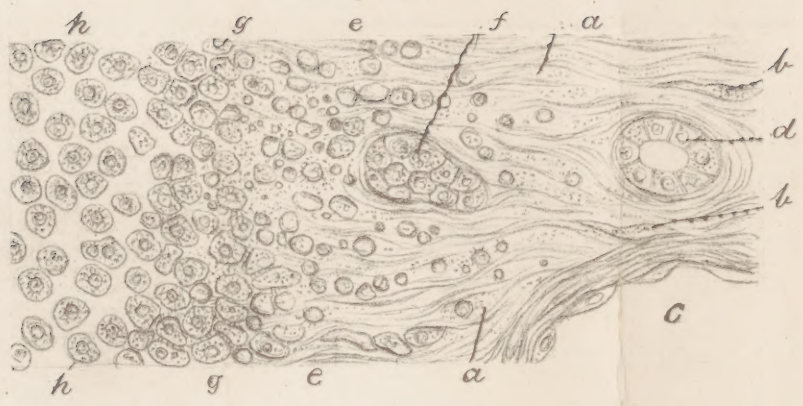


Fig. 2.



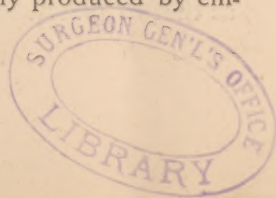
Fig. 3.



MICROSCOPICAL STUDIES ON ABSCESS OF THE LIVER.

By J. C. DAVIS, M.D.

IN vol. xxvii of the *New York Med. Journ.*, I published some clinical observations on abscess of the liver, and took the ground that, in all probability, abscess of the liver was due in most, if not in all cases, to an inflammatory process in some of the organs of the abdominal cavity, from which the radicles of the portal system take their rise, excepting, of course, those cases which are due to a parasitic origin (*Echinococcus*). Abscess of the liver seems to follow only embolism in the portal vein. These embolisms are due to transported particles of pus or shreds from the wall of some pus cavity, which being carried into the portal system, produce either suppurative phlebitis in the *porta hepatis*, the so-called *pyle-phlebitis*, or suppurative process in any part of the liver in which an embolus may have lodged. The question why pus or tissue in suppuration, if transmitted into a healthy tissue, should again produce suppuration, cannot be satisfactorily answered. We know that pyæmia, which is invariably due to a primary suppurative process on the outer surface of the body, or in an internal organ, is very commonly accompanied by multiple abscess in the liver. The conclusion that such abscesses are mainly produced by em-



bolism of pus, gains ground, if we consider the fact that pyæmia will never ensue unless suppurative phlebitis be present in the neighborhood of the primary suppuration.

My microscopical studies of abscess of the liver have been made on sections from a case of multiple abscess produced by pyæmia, the liver being crowded with inflammatory foci, some of which are broken down into abscesses. Sections from this liver, if viewed with a power of one to two hundred diameters, exhibit innumerable foci of inflammation. Some are yet in the earliest stage, and others in full suppuration. In so far as conclusions may be allowed from neighboring analogous formations, the history of suppurative inflammation of the liver is, I think, plain.

It is, in my opinion, beyond question that all inflammatory foci have their seat in the interstitial tissue, built up by the relatively small amount of connective tissue, which heretofore has been called "Glisson's capsule," and which accompanies all the branches of the portal vein, the hepatic artery and the bile ducts. It is well known that this connective tissue does not in the human liver enclose the single lobules, but is present only in a limited portion of the circumference of the lobules.

The inflammatory foci vary greatly in extent. Some consist merely in a slight infiltration of the interstitial connective tissue; others occupy the whole amount of interstitial tissue between several lobules, while others are produced by both involution of the interstitial tissue and the lobules themselves. Lastly there are inflammatory foci, in which no distinction between interstitial connective tissue and epithelial tissue of the lobule is possible, but all look granular with a low power, which means, that there have already formed, or are forming, small abscesses.

The origin of abscess of the liver is evidently the same as that of plastic interstitial hepatitis and miliary tubercu-

losis of the liver; although the termination is entirely different in the three kinds of inflammatory process. In the process termed plastic interstitial hepatitis, the termination consists in a new production of dense fibrous connective tissue, the result being that which we call cirrhosis of the liver. In tuberculosis the inflammation leads to a complete loss of blood-vessels in certain territories, with the result of shrinkage of the inflammatory elements, originating from all the tissues in a circumscribed territory. They become separated and isolated, thus producing that which we call a tubercle or a dry abscess.

As to the origin of the inflammatory elements in cirrhosis, Heinrich Müller* has made accurate studies. He has demonstrated that not only the interstitial connective tissue and the capillary blood-vessels are transformed into inflammatory elements, but that the liver epithelia also share in the formation of such elements, through the increase of the living matter in their bodies. The result of this is a recurrence of the formation of indifferent or medullary corpuscles. All these corpuscles remain uninterruptedly connected with each other, become spindle-shaped and are partly transformed into basis substance, so as to produce a considerable amount of fibrous or homogeneous dense connective tissue. Thus the participation of the liver epithelia in the inflammatory process fully explains why in cirrhosis many of the lobules are so considerably reduced in size, while the newly formed connective tissue, which very soon retracts, is so notably and greatly augmented.

The objections which might be raised against Müller's conclusions, are based merely upon hypothetical grounds, viz., that epithelia would never produce connective tissue and that on the contrary connective tissue never would produce epithelia. This objection falls to the ground in con-

* Sitzungsber. der K. K. Akad. der Wissenschaft., in Wien., 1876.

sideration of the fact that in the earliest stages of embryonal development, there are present indifferent or medullary elements only, from which all future tissues must necessarily arise.

As to the origin of the inflammatory elements in tuberculosis of the liver, direct observations are wanting. It is reasonable to conclude, however, that in tuberculosis just as well as in cirrhosis, the liver epithelia themselves furnish a large amount of medullary tissue, which, owing to the absence of blood-vessels, shrivel, become disintegrated and exhibit the crumbly material termed yellow tubercle. I have met with a case of tuberculosis in the liver of a duck, in which some of the lobules were partly, others entirely transformed into yellow tubercles, evidently through the participation of the epithelia in the production of indifferent elements.

As to suppuration of the liver, my studies have led me to the conviction that, although the inflammatory process commences in the interstitial or connective tissue, soon thereafter the epithelia also become involved, taking their part in the formation of indifferent or medullary elements. In order to illustrate, what I wish to say on the morbid changes within the protoplasm of the epithelia of the liver, I must briefly recapitulate C. Heitzmann's discovery of the structure of protoplasm in general. These observations were first published in 1873, in the transactions of the Imperial Academy of Sciences in Vienna. It would be but presumption on my part to attempt a defence of the correctness of Heitzmann's views, when so many of the ablest microscopists of the old world have already accepted them. Actual observation has satisfied me of the existence of this reticulum; my deductions respecting it may be erroneous, but the microscope certainly cannot make visible that, which does not exist.

According to this author's views each protoplasmic body,

the formerly so-called cell, is built up by a delicate reticulum, the points of intersection of which are the formerly so-called granules of the protoplasm. The nucleus, eventually the nucleolus, is but a larger granule, inasmuch as the reticulum is in close connection with both the nucleus and the nucleolus. This reticulum is living matter and flat layers of the same matter also build up the shell of the nucleus and the bounding layers of the protoplasmic lump. In connective tissue of any description the protoplasmic bodies (formerly so-called cells), exhibiting the reticular structure, send delicate offshoots into the basis substance, which being formations of the living matter, produce a reticulum within the basis substance, somewhat wider than that of the protoplasmic bodies themselves. In the meshes of the protoplasm there is present a lifeless fluid, while in the basis substance of the connective tissue the meshes of the reticulum contain a solid mass, which has evidently arisen from the former protoplasmic fluid.

Through the reticulum of living matter which pierces the basis substance everywhere, all protoplasmic bodies are brought into uninterrupted connection. The old cell doctrine, which has suggested that the animal body is built up like a dwelling with innumerable individual bricks, put together by the cement of the inter-cellular substance, has fallen to the ground. The new doctrine suggests that in the body the living matter is in uninterrupted connection and that the whole body as such represents the individual, which is traversed by closed spaces (blood and lymph vessels) containing isolated protoplasmic bodies (blood and lymph corpuscles). The plan of organization is the same as in an individual *amœba*, in which there may appear temporarily at least, closed spaces, so-called vacuoles, in the fluid of which there may float about, isolated particles of living matter.

In epithelial and endothelial layers the single elements are protoplasmic bodies, flattening each other and separated from each other by the cloak of the horny cement-substance. This cloak, however, does not isolate the protoplasmic bodies, as the cements-ubstance is everywhere traversed by delicate conical threads, the so-called thorns, which are the bridges of living matter uninterruptedly uniting all neighboring epithelia and endothelia. These, therefore, form continuous layers of living matter, which by means of delicate offshoots of the same matter, are also in direct union with the subjacent formations of connective tissue.

If this doctrine be correct, we shall see in the inflammatory process that the living matter, owing to the increased afflux of nourishing material, must be augmented and from it must arise all elements heretofore termed inflammatory corpuscles. In inflammation, however, the newly-formed elements may remain in uninterrupted connection, thus representing a tissue. If, on the contrary, the inflammatory elements be separated from each other by being torn apart, the result will be pus from the broken down tissue, and the sum total of the pus corpuscles together with a certain amount of serous fluid, will go to make up that which we call abscess.

In the earliest stages of interstitial hepatitis, marked only by slight changes of the connective tissue, we see with higher powers of the microscope (1000-1200 diameters) that the protoplasmic bodies,—the connective tissue cells—are coarsely granular; the nucleus is hidden by the coarse granules, or it is visible in the shape of a shining homogeneous globule of living matter. Such globules, of varying size, are also scattered throughout the fibrous basis substance and have evidently originated from particles of living matter, which in the normal condition produce the living reticulum in the basis substance. Such formations appear

in the largest number around the blood-vessels, both arteries and branches of the vena portæ. Next we see that the fibrous basis substance has completely disappeared and is replaced by a large number of partly shining homogeneous, partly nucleated protoplasmic lumps, which are connected with each other by means of delicate threads. (See Fig. 1).

The transformation of normal into inflamed connective tissue has evidently taken place by liquefaction or dissolution of the basis substance and increase of the living matter held therein with the result of a new-formation of inflammatory elements. In this stage the blood-vessels in the inflamed tissue are as yet recognizable, although their endothelial walls are considerably thickened, the endothelia themselves being engaged in a lively new production of living matter; while the central lumen is first narrowed, afterwards completely lost and filled up with inflammatory elements. It is the same process of proliferation, which breaks down the portal veins, the hepatic arteries and the bile ducts; the same process, which leads to the consolidation of the capillaries within the lobules and their transformation into inflammatory elements. All these elements are originally united with each other, thus representing what we call an indifferent, or inflammatory, or medullary, or granulation tissue. In foci of inflammation, where the process has advanced up to the formation of pus, the connection of the single protoplasmic bodies is lost. Here isolated pus corpuscles are suspended in the albuminous serum, which latter in chromic acid specimens, such as I have exclusively used for examination, looks finely granular. The epithelia within the lobules of the liver at the same time share in the inflammatory process in a very marked way. Firstly they undergo changes, as first described by Heinrich Müller in the above quoted publication. They swell up; the cement substance becomes invisible between a number of proto-

plasmic bodies, which now look like large irregular clusters. Necessarily, with the loss of the cement-substance goes also the loss of a number of bile capillaries. The epithelia and the protoplasmic bodies arising therefrom, become coarsely granular with their living matter augmented to such an extent that the nuclei are mostly concealed; they have in part also become increased in size, shining and homogeneous. Many of the granules assume the shape of nuclei and throughout the whole cluster new lines of demarkation appear, which lead to the formation of relatively small lumps of protoplasmic bodies, viz., inflammatory elements. All these elements are first directly connected with each other by delicate threads and in this condition represent an indifferent tissue, closely resembling that formed from the connective tissue. Lastly, however, these medullary elements are completely separated from each other and now represent pus corpuscles. (See Fig. 2.)

The transformation into pus may be localized in the interstitial connective tissue alone; or it may involve the interstitial connective tissue and a portion of the neighboring lobules; or, lastly, a large territory of the liver-tissue being engaged in the inflammatory process, breaks down into pus. The result under all circumstances will be an abscess, varying only in size. As to the emigration of colorless blood corpuscles, which was thought to be the only source of pus (J. Cohnheim), I have nothing to say. The origin of pus in my specimens at least, could be satisfactorily traced from the breaking down of the tissue itself, so much so, that in my opinion the emigrated colorless blood-corpuscles, if they were present at all, could have been by no means the main source of the pus corpuscles.

Abscess sometimes forms in the liver, which is never made manifest by noticeable symptoms; the patient going on perhaps for years, and finally dying from some other disease,

or from some traumatic cause. This never happens in multiple abscess of the liver in pyæmia, as the disease is generally rapid in its course, and death its result. In a case of formation of abscess of the liver of long standing, the abscess becomes encysted. The changes leading to the formation of a sac around the abscess have been studied by myself in a specimen, in which a liver abscess of the size of a man's fist was formed on the convex surface close to the peritoneum, which was found transformed into a tough pseudo-membrane of at least 4 mm. in thickness, and closely adherent to the diaphragm.

Microscopic sections made through the pseudo-membrane and the adjacent portions of the liver, again illustrate the way in which the pseudo-membrane, or *membrana pyogena*, had been formed. It was very plain to be seen, with high powers of the microscope, that the interstitial connective tissue of the liver and the connective tissue of the peritoneum in many cases were broken down into indifferent or medullary elements, all these being in uninterrupted connection by means of delicate thorns of living matter. The epithelia of the liver were transformed into medullary tissue, in exactly the same way which I have described above, when speaking of the formation of an abscess. The difference was, that in the latter instance the medullary elements were left in uninterrupted continuity. In some places the medullary elements became spindle shaped, and were partly transformed into a basis substance, that led to the formation of a delicately striated cicatricial connective tissue. The main mass of the medullary elements, however, had been simply transformed into a homogeneous or slightly granular basis substance, with rather scanty protoplasmic bodies. With high powers the reticular structure of the basis substance was plainly visible, due evidently to the presence of the living matter throughout the whole newly-formed mass of

connective tissue. Enclosed in this mass I met with scanty capillary blood-vessels, and a large number of islands of unchanged liver epithelia, which latter had escaped the transformation into medullary elements, and became involved in the newly formed connective tissue. (See Fig. 3.)

In looking over the literature on this subject, I have found the following, which may be worthy of quotation:

"The young cells, which in local irritations fill the connective tissue interstices, ought and must, for the greater part, be regarded as having 'migrated in.' But these still remain provisionally connective tissue cells, and their place of formation were the surrounding connective tissue cells. Even to-day yet we must not look upon the connective tissue as quite unfruitful, because an experiment of v. Recklinghausen proves that even excised pieces of the cornea, under proper conditions, are capable of a moderate cell production." (Rindfleisch, p. 455, Phila. ed., 1872.)

"The pus corpuscles which usually accumulate so as to form abscesses, are almost entirely emigrants, although recent investigations render it highly probable that they may also originate by the endogenous process of the liver cells" (Green's *Pathol. and Morbid Anat.*, Phila., 1878).

Remak, Buhl, L. Oser and S. Stricker maintain "that pus corpuscles arise in various epithelia, partly by division, partly by endogenous formation, also from connective tissue corpuscles, from muscular cells, etc."

The conclusions I have arrived at through my microscopical studies on formation of abscess in the liver, are as follows:

1. The inflammation invariably starts in the interstitial connective tissue of the liver, and secondarily involves a varying amount and number of the lobules of the liver.
2. Both the connective tissue with its blood-vessels and the epithelia of the lobules, through an increase of the liv-

ing matter, become transformed into embryonal or medullary elements, thus constituting what is termed the inflammatory infiltration.

3. The medullary elements originally connected with each other by means of delicate thorns, in turn become isolated by rupture of these thorns, and now being suspended in a serous fluid, represent pus corpuscles, the sum total of which is called an abscess.

4. The pus corpuscles, therefore, are a direct offspring of the liver tissue, both connective and epithelial, and no indication could be seen of an emigration of colorless blood corpuscles, which latter may be assumed, but by no means could be directly proved.

5. On the boundary of the abscess the inflammatory tissue is transformed into a homogeneous or striated connective tissue, building a wall around the abscess. In the formation of this, also the peritoneum shares, if the abscess had formed near it.

6. Through my studies the doctrine of C. Heitzmann of plastic and suppurative inflammation has been satisfactorily corroborated. As long as the indifferent elements remain united with each other, they represent a tissue, and are ready at any time to produce a basis substance, viz., new connective tissue. On the contrary, if the indifferent elements are broken apart, they become pus corpuscles, arisen from all constituent elements of the inflamed tissue itself.

EXPLANATION OF THE PLATE.

Fig. 1. Formation of pus in interstitial connective tissue (Glisson's capsule) of the liver; *a a*, fibrous basis substance in normal condition, with protoplasmic bodies *b b*; *c*, portal vein; *d*, bile-duct; *e e*, increased living matter in shape of shining homogeneous lumps; *f*, inflammatory elements arisen from epithelia of bile-duct; *g g*, zone in which the whole connective tissue is transformed into medullary elements, all being connected by means of

delicate threads of living matter ; *h h*, zone in which the medullary of elements are torn apart and represent pus-corpuscles. Magnified 1000 diam.

Fig. 2. Formation of pus from the epithelia of a lobule of the liver ; *a a*, normal epithelia, separated from each other by the cement-substance, united by delicate thorns ; *b b*, capillaries of the lobules ; *c c*, zone in which the epithelia are coarsely granular, transformed into multinuclear lumps ; *d d*, narrowed capillaries, with swelled endothelia ; *e e*, zone of medullary elements, arisen from both epithelia of the liver and endothelia of the capillaries, all connected with each other ; *f f*, medullary elements torn asunder and representing pus-corpuscles. Magnified 1000 diam.

Fig. 3. Formation (d) of the connective tissue capsule around the abscess of the liver ; *a a*, indifferent or medullary elements, produced by inflammation of both the interstitial connective tissue and the epithelia of the lobules ; *b b*, zone in which the medullary elements became spindle shaped, and partly transformed into basis-substance ; *c c*, newly formed fibrous basis-substance with scanty protoplasmic bodies ; *d*, island of unchanged liver-epithelia. Magnified 1000 diam.

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